SUPPORT FOR THE AMENDMENTS

Newly-added Claims 24-36 are supported by the specification and the original claims.

No new matter is believed to have been added to the present application by the amendments submitted above.

REMARKS

Claims 24-36 are pending. Favorable reconsideration is respectfully requested.

The rejection of the claims under 35 U.S.C. §103(a) over Chiesi et al. (EP 0153998 A2) is respectfully traversed. The cited reference fails to suggest the claimed process.

By definition, lyophilization is a process in which primary drying is conducted at a temperature lower than the eutectic temperature of the product. As the eutectic temperature of piroxicam:β-cyclodextrin is -18 °C (see page 2 of the specification), the process is conducted at a temperature below -20 °C.

The Inventors have discovered that when working on an industrial scale, the cooling of the aqueous solution to the temperature of complete freezing, i.e., -10 °C, should be carried out very rapidly as claimed, i.e., at cooling rate equal to or higher than 1 °C/min. Only this well-defined and controlled cooling rate allows one to obtain a piroxicam:β-cyclodextrin complex characterized by complete inclusion and complete amorphization, where the piroxicam is present in the zwitterionic form.

As recognized by the Office, Chiesi et al. are completely silent regarding the cooling rate of the aqueous solution and it does not contain any teaching on how to achieve complete freezing at a cooling rate equal or higher than 1°C min. Nor does Chiesi et al. disclose the same lyophilized product as produced by the claimed process.

In addition, the executed Rule 132 Declaration submitted herewith demonstrates that when freeze-dryer shelves are pre-cooled to a temperature of -20 °C under the conditions described by Chiesi et al., β-cyclodextrin begins to re-crystallize before the complete freezing of the solution followed by de-complexation of piroxicam and partial loss of the zwitter-ionic structure. As described in the Declaration, a piroxicam:β-cyclodextrin in a 1:2.5 molar ratio was prepared by freeze-drying, pre-cooling freeze-dryer shelves at -20 °C. The starting solution reached the freezing temperature of -10C in 120 min. Thus, the cooling rate was

about 0.7 °C/min, which is less than the rate specified in Claim 24, i.e., a cooling rate equal to or higher than 1 °C/min. It was observed that at 0.7 °C/min, β-cyclodextrin started to re-crystallize with de-complexion of piroxicam when the aqueous solution reached the temperature of 50-55 °C. The results presented in the Declaration demonstrate the superiority of the claimed process.

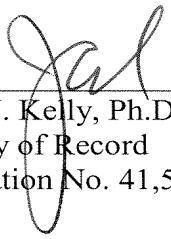
In view of the foregoing, the claimed process is not obvious of Chiesi et al. Accordingly, withdrawal of this ground of rejection is respectfully requested.

The rejection of the claims under 35 U.S.C. §112, second paragraph, and the objection to the claims are believed to be obviated by the amendment submitted above. The issues raised in the Office Action have been addressed in the newly-added claims. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.



James J. Kelly, Ph.D.
Attorney of Record
Registration No. 41,504

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 08/07)